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DIASTEREOSELECTIVE IRELAND-CLAISEN REARRANGEMENT OF ALLYLIC ALCOHOLS

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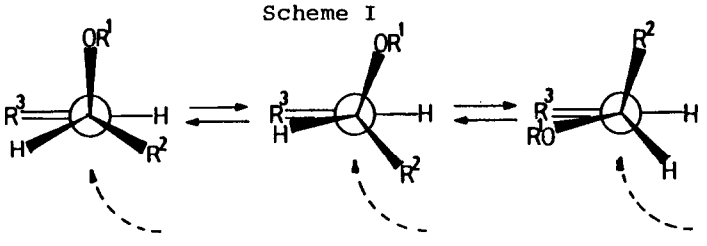
Abstract: The "chelation-controlled" Ireland-Claisen rearrangement of allylic glycolate esters is described in which the stereocontrol of the prochiral sp^2 sites is achieved by the allylic oxygen substitutent.

Recent synthetic efforts have met with considerable progress in finding general solutions to acyclic asymmetric induction.[1] Among other methods available a useful approach to the diastereoselective reactions was derived from the conformational and steric effects of the allylic substrates.[2] Empirical models for this π-facial stereoselectivity were also suggested by ab initio calculations (Scheme I).[3]

We expected the remarkable stereoselectivity observed in the osmylation of allylic alcohols and their derivatives[2d,e] would be applicable to other types of reactions including pericyclic reactions.[4] We now report the successful realization of such an approach in the Claisen rearrangement of allylic alcohols.

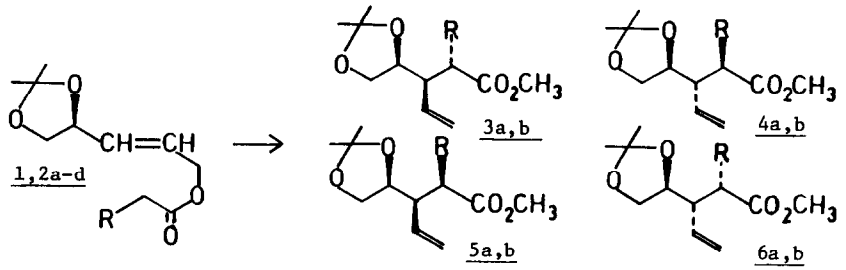
Scheme I



Thus, the "chelation-controlled" ester-enolate version[5] of the Claisen rearrangement of allylic glycolate esters was carried out with lithium diisopropylamide (THF,-100°C) followed by trimethylsilylation and warming to room temperature. After the standard workup, the diastereomeric ratios were determined by the appropriate methods (Table).

Extensive studies of the "chelation-controlled" Ireland-Claisen rearrangement have firmly established the relative vicinal stereochemistry in the products (controlled by a chair-like cyclic transition state);[5] therefore, the "anti" effect was first probed in the Claisen rearrangements of the acetates 1a and 2a, which did not exhibit any significant diastereoselective preference (entries 1 and 5).[6] As expected, however, rearrangements of the glycolate esters with increased steric demands resulted in moderate diastereoselectivities (entries 2-4 and 6-8). For these entries initially the "anti" effect in the rearrangement products was identified by their degradation to the acetate[7] and comparison with the authentic

Table

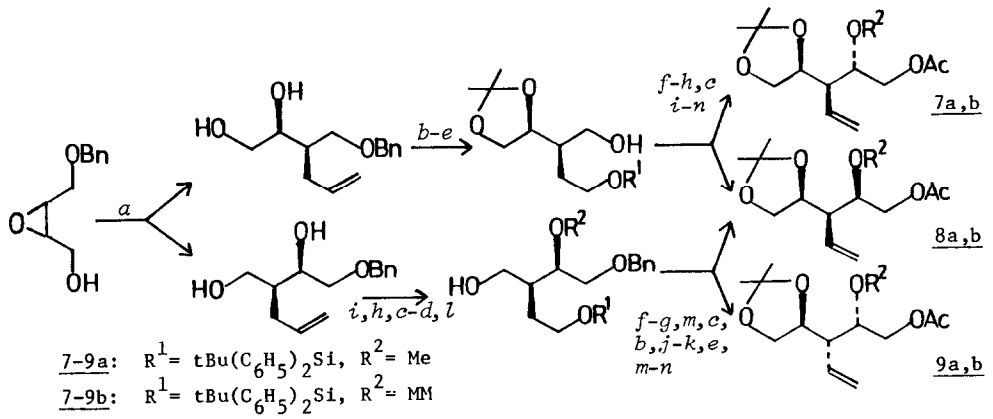


entry	substrate	double bond	R	yield[a,b]	ratios[a] (3 : 4 : 5 : 6)
1	1a	trans	H	54%	1 : 1.3[c]
2	1b	trans	OCH_3	59%	4.4 : 1 : 0.2 : 0.3[d]
3	1c	trans	OCH_2OCH_3(OMM)	50%	4.0 : 1 : 0.3 : 0.2[d]
4	1d	trans	$OCH_2C_6H_5$(OBn)	48%	4.2 : 1 : 0.3 : 0.1[d,e]
5	2a	cis	H	50%	1 : 1.4[c]
6	2b	cis	OCH_3	48%	0.5 : 0.3 : 9 : 1[c,d]
7	2c	cis	OCH_2OCH_3(OMM)	51%	*ca.* 0.1 : 0.2 : 1:(0.2)[d,f]
8	2d	cis	$OCH_2C_6H_5$(OBn)	56%	0.3 : 0.3 : 5 : 1[d,e]

a. not optimized; *b*. isolated yield; *c*. determined by capillary(SE30 50M) GC; *d*. determined by integration of peaks (δ 2.4∿2.9 ppm) in 400 MHz ^1H NMR; *e*. determined by analytical (reverse-phase) HPLC; *f*. could not be measured accurately.

sample.[6] The stereochemistry was then unambiguously determined by independent syntheses of the alcohols corresponding to 3, 5 and 6 (Scheme II).[8]

Scheme II

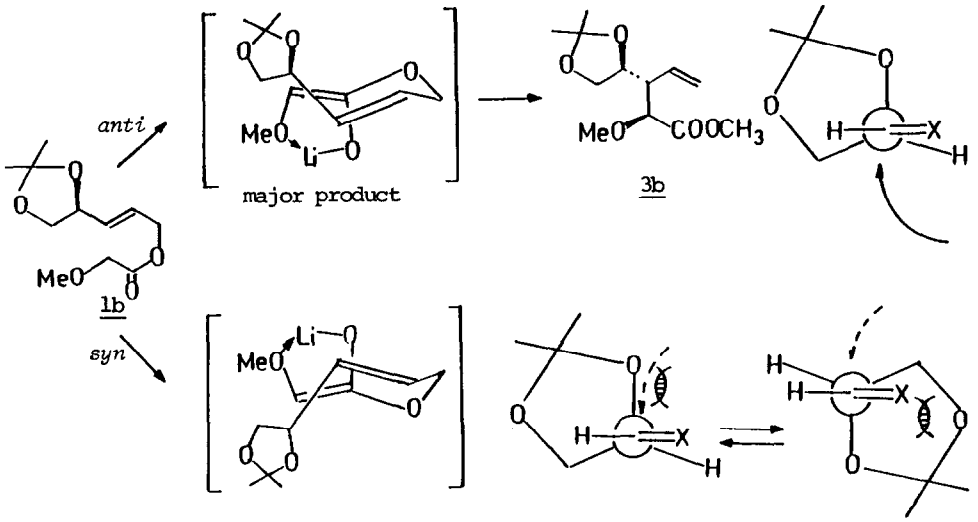


7-9a: R^1= $tBu(C_6H_5)_2Si$, R^2= Me
7-9b: R^1= $tBu(C_6H_5)_2Si$, R^2= MM

(a) CH_2=$CHCH_2MgBr$, CuI(cat); (b) $CH_3C(OCH_3)_2CH_3$, CSA; (c) $O_3/NaBH_4$; (d) $tBu(C_6H_5)_2SiCl$, imidazole, DMF; (e) Li, NH_3; (f) Swern oxid.; (g) $CH_2CHMgBr$, toluene; (h) NaH, CH_3I; (i) tBuCOCl, pyr, 0 °C; (j) $nBu_4N^+F^-$; (k) o-$NO_2C_6H_5SeCN$, nBu_3P/ 30% H_2O_2; (l) LAH, ether; (m) Ac_2O, pyr; (n) TLC separation.

In summary the relative stereochemistry between the asymmetric alkoxyl group and the adjacent newly formed C-C bond of the major rearrangement product in all examples is "*anti*" (*erythro*) (Scheme III).

Scheme III



Given ease of introduction, removal and further elaboration, the enantiomerically pure acetonide group or its derivatives can function as a chiral auxiliary; thus this methodology constitutes a new and efficient synthesis of chiral α-hydroxy and α-alkoxy acids. We believe this powerful stereocontrol of the prochiral sp^2 reaction sites by the allylic oxygen substituent is a general phenomenon and can be extended to electrophilic, nucleophilic and radical attacks as well as other sigmatropic rearrangements.[3,4,10,11]

In conclusion, although the origin of this diastereoselection still remains an open question, it suggests a general strategy by which acyclic stereochemical control can be achieved. Appropriate experiments are underway to delineate the scope and limitation of the preliminary concept educed here. Applications to natural product syntheses are currently in progress as well.

Acknowledgment: Financial support from Vanderbilt University (NSC and University Research Council) is gratefully acknowledged.[12]

References and Footnotes

1. For general reviews, see (a) D. A. Evans, J. V. Nelson, and T. R. Taber, Top. Stereochem., 13, 1 (1982). (b) P. A. Bartlett, Tetrahedron, 36, 2 (1980).
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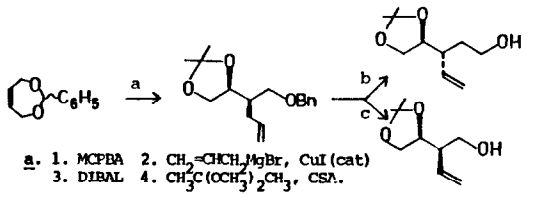
3. M. N. Paddon-Row, N. G. Rondan, and K. N. Houk, J. Am. Chem. Soc., 104, 7162 (1982) and references cited therein.
4. Recently three examples of diastereofacially selective cycloadditions appeared in which the anti-approach in a Felkin type transition state was evoked to rationalize their

results; (a) R. W. Franck, T. V. John, and K. Olejniczak, J. Am. Chem. Soc., 104, 1106 (1982). (b) A. P. Kozikowski and A. K. Ghosh, ibid., 104, 5788 (1982). (c) P. DeShong and J. M. Leginus, ibid., 105, 1686 (1983).

5. (a) R. E. Ireland, S. Thaisrivongs, N. Vanier, and C. S. Wilcox, J. Org. Chem., 45, 48 (1980). (b) R. E. Ireland, S. Thaisrivongs, and C. S. Wilcox, J. Amer. Chem. Soc., 102, 1155 (1980). (c) P. A. Bartlett and J. F. Barstow, J. Org. Chem., 47, 3933 (1982). (d) P. A. Bartlett, D. J. Tanzella, and J. F. Barstow, ibid., 47, 3941 (1982). (e) T. Sato, K. Tajima, and T. Fujisawa, Tetrahedron Lett., 24, 729 (1983). (f) S. D. Burke, W. F. Fobare, and G. J. Pacofsky, J. Org. Chem., 48, 5221 (1983). (g) J. Kallmerten and T. J. Gould, Tetrahedron Lett., 24, 5177 (1983).

6. The stereochemistry of the rearrangement products was established by their LAH reduction of the corresponding alcohols and comparison with the authentic sample.



a. 1. MCPBA 2. CH_2=$CHCH_2MgBr$, CuI(cat) 3. DIBAL 4. $CH_3C(OCH_3)_2CH_3$, CSA.

b. 1. $O_3/NaBH_4$ 2. $tBu(C_6H_5)_2SiCl$, imidazole, DMF 3. Li, NH_3 4. Swern oxid. 5. $CH_2=P(C_6H_5)_3$, THF 6. $nBu_4N^+F^-$.

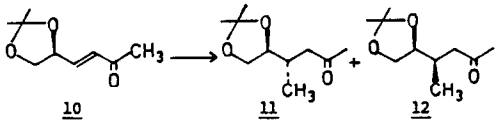
c. 1. $O_3/NaBH_4$ 2. o-$NO_2C_6H_5SeCN$, nBu_3P 3. 30% H_2O_2 4. Li, NH_3.

7. This transformation was performed in 4 steps: 1. MeLi, Et_2O, 2. MCPBA, Na_2HPO_4, CH_2Cl_2, 3. LAH, Et_2O, and 4. Ac_2O, pyr.

8. (a) For the sake of convenience only the one enantiomer is shown for all drawings; (b) Vinyl cuprate openings of α- and β-epoxides from (S)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-(E)-2-propen-1-ol were found to be capricious and also suffered from poor regioselectivity.

9. For example, see N. Minami, S. S. Ko, and Y. Kishi, J. Am. Chem. Soc., 104, 1109 (1982).

10. Indeed the conjugate addition to $LiMe_2Cu\cdot BF_3\cdot Et_2O$ to the trans enone 10 afforded the corresponding adducts 11 and 12 in 56% yield (3.8:1). The observed topological bias is consistent with that found in the Claisen rearrangement and with the example recently reported by W. R. Roush and B. M. Lesur, Tetrahedron Lett., 24, 2231 (1984). [cf. M. Isobe, M. Kitamura, and T. Goto, ibid., 21, 4727 (1980) and references cited therein].



10 11 12

11. The erythro stereoselectivity found in the following electrophilic reactions can be explained in a similar manner; (a) G. Nakaminami, M. Nakagawa, S. Shioi, Y. Sugiyama, S. Isemura, and M. Shibuya, Tetrahedron Lett., 3983 (1967). (b) A. R. Chamberlin, M. Dezube, and P. Dussault, ibid., 22, 4611 (1981) [cf. P. A. Bartlett and J. Myerson, J. Am. Chem. Soc., 100, 3950 (1978)]. (c) V. S. Martin, S. S. Woodward, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, ibid., 103, 6237 (1981).

12. We are indebted to Professors C. M. Harris, T. M. Harris and D. E. Pearson for their assistance with HPLC, NMR and GC measurements, respectively.

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